REMARKS

The foregoing amendments are respectfully submitted in response to the official action dated January 27, 2006, herein. While applicants respectfully submit that the aforementioned official action and the rejections contained therein are inappropriate in this case, and that all of the claims in this application are patentably distinguishable from the prior art cited therein, it is further submitted that the above-noted amendments to claims 67, 76, 85,89, 91, 94, 98, 103, 107 and 118 clearly place all of these claims in condition for immediate allowance, and such action is therefore respectfully solicited. Finally, it is also noted that claims 114-117, and 119 have not been rejected on any basis, and it is therefore presumed that the Examiner believes that at least these claims are patentable herein. Furthermore, claim 118 has only been rejected under § 112, which rejection is no longer appropriate in view of the amendment of that claim, and claims 89, 90, 94-111, and 113 have only been rejected over the Mantelle *et al.* '022 patent which, as is demonstrated below, is not a proper reference hereagainst. Therefore, all of these claims are also clearly in condition for allowance.

Claims 67-76, 79-88, and 91-93 have been rejected as being obvious over Miranda *et al.* '783. The Examiner repeats the prior rejection based on Miranda *et al.* '783, except that this rejection is no longer applied to claims 78, 89, 90, 94-99, 103, and 114, and the Examiner no longer contends that the polymers shown in Miranda meet the limitations of claims 89, 94, 103, and 114 because applicants' two claimed monomers; namely, a C_1-C_4 alkyl acrylate and a C_4-C_{12} alkyl acrylate, collapse to one monomer for C_4 because the ranges overlap C_4, nor that, as to the claimed drying temperature of 100°F, propylene glycol has a

boiling point exceeding that temperature. Instead, the Examiner now states that applicants argue that no teaching excludes solvents which are not driven off during drying, but that the process of making is not considered to be a patentable limitation during prosecution of composition claims. As for the solvents of claim 76, the above-cited solvents were said to volatilize at a sufficiently high drying temperature. This rejection is respectfully traversed in view of the above amendments and arguments and for the reasons set forth hereinafter.

The Examiner has withdrawn the prior contention that the limitations of claims 89, 94, 103, and 114 are met by Miranda *et al.* '783. Such a contention would clearly be inappropriate in view of the previous amendments to those claims, and the fact that the claimed alkyl acrylate components no longer overlap, since the claims now clearly require each of the two components set forth therein. Furthermore, the Examiner no longer states that propylene glycol has a boiling point above those specifically claimed in these drying systems, such as above 100°F. This is certainly understandable, particularly in view of applicants' having pointed out that propylene glycol does have such a boiling point, and that this is precisely why Miranda *et al.*'783 neither teaches nor suggests the presently claimed invention. The present invention thus allows one to tailor the release rate of the claimed highly plasticizing drugs (namely, those which are of low molecular weight and liquid at or about room temperature), as well as their permeation rate through the skin, by dealing with the overall nature of these transdermal systems, and the solvents utilized therein, and by not focusing solely upon the specific adhesive utilized therein. Thus, in accordance with this invention, the only solvents used

in producing therapeutic adhesive formulations which include a highly plasticizing drug are relatively high volatility solvents such as ethanol, which are removed upon drying, as are those solvents found in the adhesive polymers themselves for the prevention of *in situ* crosslinking, and/or to maintain the adhesive in liquid form until their removal. Less volatile solvents such as propylene glycol, however, which remain in these systems even after drying at these temperatures, as is specifically discussed in the specification at paragraph [0026], are specifically excluded from the presently claimed adhesive formulations. Thus, since Miranda *et al.* '783 specifically teaches one to utilize such solvents makes it abundantly clear that this reference cannot be said to somehow teach one to exclude these solvents. Miranda *et al.* '783 clearly teaches away from the present invention.

In place of these prior arguments, the Examiner now contends that the limitations in these claims do not actually exclude these solvents, since they are allegedly "process of making" limitations. Applicants respectfully disagree with this contention. Claim 67, for example, as well as independent claims 76, 89, and 91, as now amended, define transdermal delivery systems which must include not only a hydrophobic adhesive polymer and a drug having low molecular weight and being liquid at or about room temperature, but which must be free of a specifically defined class of low volatility solvents. Those low volatility solvents are claimed to be any solvents which will not be driven off during drying of these systems at temperatures of from 100°F to 200°F. This is not a method limitation; this is a specific definition of solvents, with specific properties, which are excluded from the claimed systems

of the present invention. Claim 67 thus specifically excludes compounds such as propylene glycol, which the Examiner himself admits would not be driven off at temperatures between 100°F and 200°F. It is, in any event, clear beyond question that the limitations in claims such as claim 67 specifically define the low volatility solvents therein. These are solvents which have properties, *i.e.*, a boiling point, which prevents them from being driven off during drying at temperatures of from 100°F to 200°F. Indeed, the Examiner would clearly not even be making this rejection if the language in these claims instead stated that the solvents have a boiling point between 100°F to 200°F, yet this is essentially what these claims presently state. It is therefore respectfully submitted that these limitations must be considered by the Examiner since they are clearly positive limitations upon these claims, and they render these claims fully patentable over the prior art.

Claims 67-70, 72, 73, 76, 79, 81, 82, 85-88, and 91-93 have been rejected as being unpatentable over Sablotsky. The Examiner repeats verbatim the prior rejection over Sablotsky, except that this rejection is no longer applied to claims 89, 90, 94-99, and 101-110. The Examiner does not specifically respond to any of the arguments presented in applicants' prior opposition to Sablotsky. Without repeating each of these arguments, and again referring to claim 67, for example, it has been previously noted that Sablotsky does not even recognize the fact, in systems with hydrophobic adhesive polymers (such as acrylates), and in which a drug is employed which is of low molecular weight and liquid at or about room temperature, that it is highly advantageous to maintain these systems substantially free of low volatility solvents which are not

driven off during drying at the presently claimed temperatures. Once again, the Examiner had previously noted that this patentee includes such solvents, such as propylene glycol, which are specifically excluded from the present claims. Again, the Examiner has not responded to these contentions, which are clearly correct. To the extent that the Examiner's repeated position with respect to Sablotsky depends upon one ignoring the limitations in claims such as claim 67 with respect to the definition of the low volatility solvents excluded therefrom, applicants' previous position is repeated; namely, that these claims are strictly limited to and exclude from their scope solvents such as the propylene glycol disclosed in Sablotsky, and therefore clearly distinguish thereover. Similar arguments also apply with respect to claims 76, 85, and 91.

Claims 1-3, 5, 8-10, 12-15, and 18-28 have been rejected as being anticipated by Lhila *et al.* It is noted that, although the Examiner repeats the specific allegations previously made with respect to Lhila *et al.*, this rejection is no longer applied to claims 67, 69, 70, 72, 73, 76, 78, 79, 81, 82, and 103-105. The Examiner also argues that, while applicants argue that Lhila *et al.* does not teach the claimed solvent properties, such properties must be possessed by the anticipatory composition because it is the same as that claimed. This, of course, is not correct. As applicants have previously pointed out, the Lhila reference is specifically directed to the use of a particular appetite-suppressant drug known as phenylpropanolamine HCl (*i.e.*, PPA). The Lhila patent is thus concerned with the fact that this particular drug has not been found to easily permeate human skin, and thus has been problematic with respect to potential use in transdermal

applications. The invention of Lhila is said to be based upon a finding that PPA may be combined with a carrier adhesive and a combination of permeation enhancers to provide transdermal delivery systems. The adhesive systems are said to be known, and include acrylic pressure-sensitive adhesives, including Gelva 788. The permeation enhancers which are required by this patent include polypropylene glycol and the like. The disclosure of Lhila is quite distant from the overall nature and substance of the invention presently claimed in claims 1 *et seq.*

Turning to claim 1, this claim requires an active agent in protonated form, a nonaqueous solvent which is capable of dissolving a drug in either its protonated or non-protonated form, and a biocompatible deprotonating agent having the required properties of claim 1. The Examiner points to the fact that the disclosure in Lhila *et al.* includes a requirement for a pH control additive, such as Trolamine 85NF, which is a triethanolamine product. Triethanolamine is indeed one of the deprotonating agents specified in the present specification. However, this does not render the Lhila *et al.* reference anticipatory since it does not even disclose the basic concept of claim 1; namely, use of a nonaqueous solvent which can dissolve the pharmaceutically active agent in either its protonated or nonprotonated form, along with the biocompatible deprotonating agent itself. This failure is understandable, however, since the invention in Lhila *et al.* merely claims that the PPA can be mixed with certain permeation enhancers and pH control additives to assist it in transference through the skin. There is no disclosure in this reference of the specific claimed combination of claim 1, nor of any combination which includes a drug in protonated form, a nonaqueous solvent which can dissolve

the drug in both its protonated or nonprotonated form, as well as a biocompatible deprotonating agent itself. It is therefore clear that the Lhila reference neither teaches nor suggests the specific invention set forth in claims 1 *et seq*.

Claims 1-9, 11-14, 16-28, and 67-84 have been rejected as being obvious over Wolter *et al*. Once again, the Examiner essentially repeats the prior position taken with respect to this reference, with the exception that it is no longer applied to claims 94-121. The Examiner adds that applicants argue that glycerol does not meet claim 67. It is noted, however, that it will volatilize at a sufficiently high drying temperature, and that ethyl acetate and ethanol meet the claim limitations as to volatility. This rejection is respectfully traversed in view of the above amendments and arguments and for the reasons set forth hereinafter.

The Wolter *et al*. reference is directed to pharmaceutical substances which are chemically basic in nature. These include selegiline, as well as propranolol, which are said to be volatile under ambient conditions, but which is clearly not the case with respect to propranolol. As has been noted previously, propranolol is a crystalline solid at room temperature. The invention of Wolter *et al*. is then said to comprise a transdermal patch for these allegedly volatile pharmaceutical ingredients of chemically basic nature comprising a multi-element system of a matrix of pressure-sensitive adhesive which includes a salt or contains basic groups to liberate the free base from its salt. Thus, the product is produced by mixing the physiologically acceptable salt of the active agent and a fluid composition of a pressure-sensitive adhesive with a solvent or diluent, followed by evaporation to produce a matrix of homogeneous substrate in layer or

particulate form. The solvent thus appears to be used to dissolve the drug and mix it with the adhesive prior to its removal. A separate second layer is then formed of a deprotonating agent, as well as a solvent and adhesive, and the solvent is then once again removed. Of course, the invention of claim 1 does not require the two separate layers which are essential to Wolter *et al.* In any event, however, Wolter *et al.* specifically discloses the fact that when a salt of the drug is utilized the ability for it to diffuse may be improved by concomitant use of a conventional solubilizer "such as glycerol, 1,2-propanediol, the monomethyl or monoethyl ether of diethylene glycol, 2-oxtyldodecanol, the laurate, palmitate, stearate or oleate of sorbitol, C_8/C_{10} ethoxylated glycerides, and ethoxylated oleic glycerides." (Col. 2, lns. 54-58.) It is thus clear, particularly with respect to claims such as claim 67, that far from disclosing compositions which are substantially free of low volatility solvents which are not driven off during drying, this patentee requires the incorporation of such solvents into the systems thereof. Similarly, at column 3 of Wolter *et al.*, where the patentee describes his second layer (b), it is once again urged that this composition include compounds which would not meet the limitations of the present claims, and which thus comprise the very same nonvolatile solvents which are specifically excluded by the language of these claims. Again, all of these claims are therefore clearly patentable over the prior art.

Claims 94-102, 104-111, 113, and 118 have been rejected under 35 U.S.C. § 112, second paragraph. However, with respect to each of these rejections, the above-noted amendments to the respective claims are believed to clearly obviate these

rejections, which are therefore believed to no longer be appropriate. Thus, the above amendments to claims 94, 98, 113, and 118 are believed to obviate this rejection.

Claims 1-14, 17-21, 24-28, 67-111, and 113 have been rejected as being anticipated by Mantelle '022 under 35 U.S.C. § 102(e). Mantelle '022 is said to teach a transdermal product comprising a liquid active, a polymer, and DURO-TAK 87-2852 is disclosed, which is said to be the same polymer as applicants teach. Selegiline is also said to be disclosed, propranolol is specified, and propylene glycol is said to be disclosed therein. Rubber and polysiloxanes are disclosed, as are 10-90% acrylate and 1-40% drug. Ethanol and ethyl acetate are also said to be disclosed, and 15% selegiline is specified, as is urea. This rejection is respectfully traversed in view of the above amendments and arguments and for the reasons set forth hereinafter.

Firstly, attached hereto is a copy of the Declaration under Rule 131 swearing behind the Mantelle '022 reference which was filed in applicants' parent Application No. 08/883,075. Indeed, a similar rejection to the claims in that parent application has been interposed by the Examiner. It is thus applicants' position that Mantelle '022 is not a proper reference against the presently pending claims under any provision of § 102. In attempting to apply the provisions of § 102(e) to these claims in the face of this declaration, the Examiner's position has been that the declaration is inapplicable because the present application and Mantelle '022 are claiming the same invention. However, the fact that this is not the case in the present situation is even clearer than was the case in applicants' parent application. Most of the claims which have been rejected under § 102(e) in this case are far

different from the claims in Mantelle '022, again even more so than was previously the case. For example, claim 1 in this application is directed to a therapeutic adhesive formulation which includes an adhesive material as well as a pharmaceutically active agent in protonated form, a nonaqueous solvent for dissolving the active agent in either its protonated or unprotonated form, and a biocompatible deprotonating agent. The claims in the '022 patent bear very little, if any, relationship thereto, and if the claims are not directed to the same invention, then the Rule 131 declaration effectively removes Mantelle '022 as a legitimate reference hereagainst. Apart from claim 1, claims 67, 76, 85, and 91, and the claims dependent thereon, are also patentably distinguishable from the invention claimed in Mantelle '022. Most significantly, there is no teaching or suggestion in the claims of Mantelle '022, including claim 23 thereof, that the transdermal delivery systems of the present invention can be prepared by essentially eliminating a certain class of solvents from these systems; namely, those which will not volatilize during drying at temperatures of from 100°F to 200°F. Finally, claims 91 and 103 are also clearly distinguishable from the claims in Mantelle '022. These claims are directed to specific therapeutic adhesive formulations, including a specified combination of acrylic polymeric adhesives including the required hardening monomer, along with a functionalizing monomer facilitating crosslinking, as well as the highly plasticizing drug component thereof. Once again, claim 23 of Mantelle '022 nowhere teaches or suggests these claimed inventions. Applicants submit, in fact, that the Examiner's "shotgun" approach to the application of Mantelle '022 under § 102(e) proves that this position is

entirely improper. The Examiner's position seems to be that any claim which could somehow employ a single polymer component (*e.g.*, DURO-TAK 87-2852), irrespective of the overall nature of the claimed invention, must be directed to the "same invention." Even the Examiner will realize the impropriety of such a position.

In applicants' parent application, the Examiner has applied the "two-way test" in determining this issue; namely, whether the claims pending in the present application are patentable over claims such as claim 23 of Mantelle '022, and *vice versa*. *See Winter & Fujita*, 53 U.S.P.Q.2d 1234, 1243 (Bd. Pat. App. & Interf. 1999). From the point of view of claim 23 of Mantelle '022, the invention claimed therein is quite different from that of the presently pending claims in that it is specifically directed to an adhesive polymer which consists of acrylic-based polymers which are required to have a specified shear resistance so that they can maintain sufficient tack and shear to remain in place during use, irrespective of which solvents are employed therewith. The thrust of the invention of claim 23 in Mantelle '022 is thus to select a particular acrylic adhesive which has certain specific properties in order to allegedly obtain these results. Turning to the claims in the present application, as noted above, these claims are directed to an entirely different invention. Claims 1-14, 17-21, and 24-28 are directed to therapeutic adhesive formulations as discussed above, including both a pharmaceutically active agent in protonated form, and a biocompatible deprotonating agent which can deprotonate the active agent without causing irritation upon prolonged exposure to the skin. Claims 67, 76, 85, and 91 are directed to the use of hydrophobic adhesive polymers with certain specified highly plasticizing drugs in

systems which are substantially free of low volatility solvents not driven off drying at temperatures of from 100°F to 200°F. Finally, claims such as claims 94 and 103 are directed to the selection of a specific type of acrylic polymer combination which is thus not suggested by claim 23 of Mantelle '022. In each case, these are entirely different concepts, and even in the case of claims such as claim 67, the claimed invention is in no way based on a determination of the shear resistance of the claimed polymers, or of any polymers used therein. These differences were, in fact, highlighted during prosecution of Mantelle '022 itself. During that prosecution, a declaration was filed under Rule 132 comparing four acrylic-based pressure-sensitive adhesives; namely, DURO-TAK 87-2979, 87-1297, and 387-2553, as well as DURO-TAK 87-2852, which was said to be the one with high shear-resistance characteristics. The first three adhesives were said to be lower than minimum shear resistance. That declaration thus included a table showing that the first three DURO-TAK adhesives had a shear resistance of 24 and 2 hours, respectfully, at 4 psi at 72°F, but that DURO-TAK 87-2852 was said to be greater than 100 hours at 4 psi at 72°F (50 hours at 8 psi at 72°F). These polymers were then formulated with selegiline base and a silicon pressure-sensitive adhesive (Bio-PSA X7-4501) in the proportions set forth in the following table.

Raw Material	Ex. 1	Ex. 2	Ex. 3	Ex. 4	Ex. 5	Ex. 6	Ex. 7	Ex. 8
Selegiline Base	20	20	20	20	15	15	15	15
Bio-PSA X7-4501*	20	20	20	20	20	20	20	20
Duro-Tak 87-2852	60	-	-	-	65	-	-	-
Duro-Tak 87-2097	-	6-	-	-	-	65	-	-
Duro-Tak 387-2353	-	-	60	-	-	-	65	-
Duro-Tak 87-2979	-	-	-	60	-	-	-	65

*Silicone PSA, Dow Corning Corp., Midland, Michigan

The shear-resistance characteristics of these materials were then tested, and those with less than 2-3 minutes were generally said to be gummy and oozy compositions. The following table was said to show that Examples 1 and 5 had acceptable shear-resistance values.

Samples	Shear Values (minutes)
1	5.6
2	0.2*
3	0.7
4	0.1*
5	13.9
6	0.4
7	1.4
8	0.1

*Only one unit tested (samples delaminated/fell apart)

The claims in that application were then amended to include the same shear-resistance values.

Once again, this can be contrasted not only to claims such as claims 1 and 94 of the present application, but also to claims such as claim 67, and it is clear that claim 23 in Mantelle '022 does not teach or suggest the inventions to which all of these claims are directed. There is nothing in claim 23 of Mantelle '022 about either the concept of utilizing an adhesive formulation in a transdermal delivery system which includes an active agent in protonated form along with a nonaqueous solvent capable of dissolving the active agent in either a protonated or unprotonated form, along with a biocompatible deprotonating agent, nor is there anything about the concept of excluding low volatility solvents which are driven off during drying at temperatures of from 100°F to 200°F

from these compositions in order to obtain the results of the present invention, nor is there any suggestion of the use of a therapeutic adhesive formulation which includes an acrylic polymer adhesive comprising both a C_4-C_{12} alkyl acrylate and a C_1-C_3 alkyl acrylate hardening monomer, along with a functionalizing monomer which facilitates crosslinking thereof.

Claim 23 in Mantelle '022, by itself, does not teach or suggest the inventions to which the present claims are directed. There is nothing in claim 23 about the inventive concept of excluding water and certain low volatility solvents from these compositions in order to obtain the results of the present invention. To the contrary, a totally different invention; namely, selection of a particular adhesive polymer with a particular shear resistance, is the sole invention of that claim. Indeed, claim 23 would certainly not suggest that the use of the very same acrylic polymers which are specifically excluded from claim 23 can actually result in compositions which have these properties by virtue of their exclusion of water and low volatility solvents. Therefore, applying the two-way test referred to by the Examiner, if claim 23 of Mantelle '022 were prior art against the claims in this application, it is respectfully submitted that the present claims would clearly be patentable over this prior art. The prior art (claim 23) would not in any way, shape or form suggest the claimed inventions of providing for transdermal delivery of a drug by utilizing that drug in a protonated form, along with a nonaqueous solvent capable of dissolving the drug in both protonated and nonprotonated forms, and a biocompatible deprotonating agent for the purposes thereof, nor the invention of excluding water and certain low volatility solvents from these compositions in order to obtain the present results, nor the invention of utilizing

the specific composition of alkyl acrylates set forth in claims 94 and 103. Indeed, claim 23 would, in fact, teach away from these inventions, such as that of claim 67, because it would clearly teach that using acrylic polymers that do not meet the requirements of claim 23 would not work. To the contrary, however, the present application proves that by employing the claimed invention hereof, it is possible to use many acrylic polymer compositions which would not meet the requirements of Mantelle '022, but which would nevertheless result in the improved results of the present invention.

On the other hand, if the present claims were prior art against claim 23 of Mantelle '022, it is submitted that claim 23 would clearly be patentable thereover because the claims in this application do not suggest that by merely selecting acrylic polymers meeting specific shear resistance requirements one can achieve the results claimed by Mantelle '022. To the contrary, the present specification is replete with data demonstrating that shear resistance is not a predictable factor in selecting the products of this invention. Products with varying shear resistance properties were actually tested in this application, and it was found that this was not a critical factor in selecting the improved products hereof. Applicants therefore assert that the two-way test establishes that these are different inventions and that there would be no interfering subject matter therebetween, that no interference in fact could exist, and that the provisions of 35 U.S.C. § 102(e) should not be applied in this case.

Beyond al of the above, however, it also appears to be the Examiner's position, in view of the sole fact that Mantelle '022 and the present application disclose a single species of acrylic adhesive (namely, DURO-TAK 87-2852), which the Examiner

contends could be used in both the claimed invention hereof and that of Mantelle '022, that this rejection is appropriate.

The Examiner cites no authority for the specific rejection over Mantelle '022 under 35 U.S.C. § 102(e), nor the refusal to accept the previously filed Declaration under Rule 131 herein. The rejection itself, however, is clearly based upon a contention that applicants and Mantelle '022 are claiming the "same invention," and therefore Rule 131 does not apply. This, in turn, is clearly based upon the allegation that the DURO-TAK 87-2852 disclosed in Mantelle '022 is the same as one polymer which is specified by applicants as being useful in the present invention. It is thus the Examiner's position that a single point of overlap between the acrylic polymers within the scope of the claims in Mantelle '022 and the acrylic polymers within the scope of applicant's claims makes it unquestionable that the "same invention" is involved in both cases. The Examiner's position is without support, either legally or logically.

Applicants have described above the many reasons why the claims in this application and those in Mantelle '022 are patentably distinct from each other. On a factual basis, however, attached hereto as Exhibit A is a specification from National Starch and Chemical Co. with respect to that company's Product DURO-TAK 87-2852 which specifies that this product has a shear strength of "at least 20 hours at 8 psi." It is therefore unclear whether, by the mere disclosure of DURO-TAK 87-2852 as one embodiment of a suitable acrylic polymer for use in the invention of that patent, that this can be said to clearly establish that the claims of Mantelle '022, such as claim 23, also clearly include this compound. If DURO-TAK 87-2852 is only disclosed in Mantelle '022, but is not claimed therein, even under the Examiner's theory, there is no barrier to the

acceptance of applicants' Declaration under Rule 131. On the other hand, if as stated by the manufacturer of that product, there is at best a variability in the shear strength of DURO-TAK 87-2852, so that it can presumably be either above or below the limits set forth in the claims of Mantelle '022, the mere disclosure of that compound in Mantelle '022 does not necessarily mean that the claims which ultimately issued in Mantelle '022 actually do incorporate DURO-TAK 87-2852. Thus, even the single point of overlap between these claims and the claims in the present application as asserted by the Examiner may not actually exist, and the Examiner will be left with absolutely no basis for applying § 102(e), even under the Examiner's apparent legal theory..

Without further authority, the Examiner's position in this case is unsupportable. The attempt to prevent applicants from swearing behind Mantelle '022 based solely upon an alleged coincidence of a single overlapping point with respect to the acrylic adhesive which is allegedly usable in each of these inventions is an entirely inadequate and improper basis for concluding that applicants and Mantelle '022 are claiming the "same invention." This is simply not the case here; applicants could not support the limitations in the claims in Mantelle '022 based on their specification; and there is simply no reason why the Declaration under Rule 131 has not been accepted in this case. If the Examiner therefore refuses to accept this position and persists in this rejection, it is respectfully requested that some authority for this specific position (namely, that a single point of overlap between one of the elements in applicants' claims and the claims in Mantelle '022 (even if one such point does exist — which applicants vehemently deny)) establishes that these two patents are claiming the "same

invention." It is believed that there is no real authority for this position.

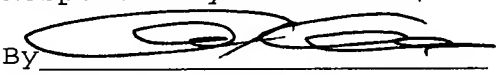
As it is believed that all of the rejections set forth in the official action of January 27, 2006, have been fully obviated, favorable reconsideration and allowance of all of the presently pending claims herein are earnestly solicited.

If, however, for any reason the Examiner does not believe that such action can be taken at this time, it is respectfully requested that he/she telephone applicant's attorney at (908) 654-5000 in order to overcome any additional objections which he might have.

If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge Deposit Account No. 12-1095 therefor.

Dated: April 27, 2006

Respectfully submitted,

By 

Arnold H. Krumholz
Registration No.: 25,428
LERNER, DAVID, LITTENBERG,
KRUMHOLZ & MENTLIK, LLP
600 South Avenue West
Westfield, New Jersey 07090
(908) 654-5000
Attorney for Applicant

643294_1

National Adhesives
A National Starch & Chemical Business

National Starch and Chemical Co.
Transdermal Technical Sevice
10 Finderne Ave.
Bridewater, NJ 08807
Phone: 908-685-7463
Fax: 908-575-7288

Customer / Address

Adhesive Specification Sheet

Date: 2/3/2006
National Approver: Paul Smutz
National Signature:
Customer Approver: Marty Fletcher
Customer Signature:
Date:

Mylan Technologies Inc.
110 Lake Street
St. Albans, VT 05478-2266
Attn: Marty Fletcher
Fax: 802-527-8151

Product No: 0872852
Cust. Prod. No/Desc.:

Product name: DURO-TAK®

The following statement will appear on all COAs:

> This COA is generated by SAP. This batch has been reviewed and approved by Quality Control.

This statement is equivalent to a signature release.

Batch 0000000000 / Quantity 0000 LB

Characteristic	Min	Max	Batch 0000000000
SOLIDS, %	31.5	35.5	%
VISC (R3,20,72)	1300	3700	cps
IR SPECTRUM	0.992	1.000	
180° PEEL ADHESION, OZ/INCH	35	75	oz/in
SHEAR, HRS (8PSI)	20	-	hrs.
RESIDUAL 2-EHA, PPM	-	1000	ppm
RESIDUAL MA, PPM	-	1000	ppm
RESIDUAL AA, PPM	-	500	ppm
MANUFACTURING DATE:			

Specification Sheet Only. This is not a COA.

PATENT
BERTEK 3.0-025

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of
Govil *et al.*

Application No. 08/883,075

Filed: June 26, 1997

For: ADHESIVE MIXTURE FOR TRANSDERMAL DELIVERY OF HIGHLY PLASTICIZING DRUGS

Group Art Unit: 1617

Examiner: E. Webman

Date: October 15, 2002

COPY

Assistant Commissioner for Patents
Washington, D.C. 20231

SUPPLEMENTAL DECLARATION UNDER 37 C.F.R. § 1.131

Sir:

1. I, Dr. Ludwig J. Weimann, am one of the co-inventors with Dr. Sharad K. Govil of the above-identified pending U.S. patent Application No. 08/883,075, filed in the United States Patent and Trademark Office on June 26, 1997.

2. I am presently a consultant for Mylan Technologies, Inc., the assignee of Application No. 08/883,075, but I was employed by Mylan Technologies, Inc. and its predecessor, Bertek, Inc., for about 20 years, and was Senior Director of Research when I retired in 1998.

3. I invented the subject matter of Application No. 08/883,075, including that of claims 84 and 92 therein, with Dr. Govil, and in accordance with our invention we reduced the invention to practice prior to June 7, 1995.

4. I am familiar with the prosecution of this patent application, including the official action dated July 23, 2002. In particular, this official action includes a rejection based upon Mantelle *et al.*, U.S. Patent No. 6,316,022 ("the '022 patent").

5. It is my understanding that the '022 patent has been applied as a reference against Application No. 08/883,075 under 35 U.S.C. § 102(e), based upon a U.S. filing date of June 7, 1995.

6. Dr. Govil and I completed the invention of claims 84 and 92 of our pending application in the United States before the filing date of the '022 patent; namely, before June 7, 1995, claims 84 and 92 reading as follows:

> 84. A transdermal delivery system consisting essentially of a blend of:
> (a) one or more hydrophobic acrylic-based polymers; and
> (b) a therapeutically effective amount of one or more drugs, at least one of which is of low molecular weight and liquid at or about room temperatures,
> wherein said system is substantially free of water and liquids having a normal boiling point (i) below processing temperatures and (ii) equal to or greater than the normal boiling points of the low molecular weight drugs.
>
> 92. A transdermal delivery system consisting essentially of a blend of:
> (a) an acrylic-based polymer; and
> (b) a therapeutically effective amount of a drug having a low molecular weight and being a liquid at or about room temperatures, wherein said system is substantially free of solvents selected from the group consisting of water and liquids having a normal boiling point
> (i) below processing temperature and
> (ii) equal to or greater than the normal boiling points of the low molecular weight drugs,
> whereby said transdermal drug delivery system, subsequent to processing, is free of said solvents.

7. In particular, prior to June 7, 1995, we were involved in the preparation of a transdermal drug delivery system for use in connection with certain drugs having a low molecular weight, such as selegiline, and their application in a system which could be adhesively applied to the skin.

8. Prior to June 7, 1995, we thus invented and actually reduced to practice a transdermal delivery system for selegiline which used selegiline in a transdermal patch using a non-aqueous solvent in connection with an acrylic adhesive polymer system and employing only solvents which were highly volatile, such as ethanol, which were removed during drying, but we excluded solvents that remained after drying, such as propylene glycol and the like.

We thus employed the low molecular weight drug selegiline, which is a liquid at or about room temperature, along with a polymer system in which the entire system was substantially free of water, as well as liquids which had a normal boiling point below processing temperatures for the patch, and equal to or greater than the normal boiling point of the selegiline.

9. Prior to June 7, 1995, under my direct supervision and control, such selegiline patches were prepared. In particular, as shown on page 77 of Notebook No. 24 (a copy of which is attached hereto as Exhibit A, with the actual dates blanked out), Susan Honn, a laboratory chemist and myself prepared a patch identified as SEL-77C employing 30 mg selegiline, in the free base form, in a 10 cm^2 patch. In the three patches shown on page 77, the patches included varying percentages of the acrylic pressure-sensitive adhesive known as GELVA 1753 (Monsanto), including 32% solid content and self-cross-linkable acrylic adhesive containing a hardening monomer comprising methyl acrylate along with ethyl acetate in the amounts shown. In particular, the acrylate adhesive GELVA 1753 was mixed with the ethyl acetate and the selegiline drug was added while mixing in order to create a homogeneous blend. A thin film of the drug/adhesive blend was then produced and applied to a release-coated plastic/paper substrate. The coating was then dried in an oven and then laminated to a backing material made of PET/PE and die-cut into patches.

10. All of the patches produced in the manner shown in Exhibit A were free of water and liquids with a normal boiling point below the processing temperature and equal to or greater than the normal boiling points of the drug utilized, and were specifically free of 1,2-propanediol as shown thereon.

11. At a subsequent date, but still prior to June 7, 1995, additional patches were prepared again using selegiline in the free base form, and in this case with and without 1,2-propanediol. These were again prepared by Susan Honn, under my direct supervision and control, and by myself. As is thus shown on pages 143 and 144 of Notebook No. 24 (copies of which are attached hereto as Exhibit B, with the dates blanked out), Examples 2 and 3

included the same GELVA 1753 (Monsanto) previously used, in combination with selegiline in free base form and ethanol. As shown in Example 3 on page 144, 1,2-propanediol was not employed, while in Example 4 it was employed. In the case of Example 3 the selegiline in the free base form was mixed with the ethanol and then added to the adhesive GELVA 1753 while mixing. In Example 4 the ethanol was added to the GELVA 1753 and the selegiline was then mixed with the 1,2-propanediol and added to the GELVA 1753 while mixing.

12. In addition, as shown on pages 152 of Notebook No. 24 (a copy of which is attached here to as Exhibit C with the dates blanked out), Robert Campbell, a lab technician, and myself conducted shear and peel tests, including those for Examples 3 and 4 from page 144. Susan Honn and myself then also calculated the coat weight for these formulations, and these are shown on page 153 of Notebook No. 24 (a copy of which is attached hereto as Exhibit D with the actual dates blanked out), including those from Examples 3 and 4 from page 144.

13. Again in each of these cases, all of which were actually carried out prior to June 7, 1995, transdermal patches were produced in which the drug delivery system included a pressure-sensitive adhesive comprising an acrylic polymer (one or more polymers) as well as selegiline in the free base form (a therapeutically effective amount of a drug which is a low molecular weight and a liquid at or about room temperatures) and in which systems were substantially free of water as well as liquids with a normal boiling point below the processing temperature for the patch and equal to or greater than the normal boiling points of the selegiline. These patches were actually produced and tested on dates prior to December 19, 1996.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United

States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

10/25/02
Date

LUDWIG J. WEIMANN

393857_1.DOC

2-10-03
Expires

Bonnie L. Coon
Notary

Project No.

TITLE Formulation of Selegiline free base Book No. 24

From Page No. patches with 30mg Selegiline / 10cm² patch

		per solids	per liquids	Y/O	(1/E)	
SEL-77A						
2.5wet 2.1dry	GMS 1430 (41% solid)	70	170.7	17.1	34.2	25.65
	1.2 PD	—	—	—	—	
	Selegiline free base	30	30.0	3.0	6.0	4.5
	Ethyl Acetate	30	30.0	3.0	6.0	4.5
	1 step GMS 1430 mix with Ethyl Acetate					
	2 step Add Selegiline while mixing.					
SEL-77B						
		70.2	per liquids	(Y/E)		
	80-1194 / 47% solids	~~149.0~~	149.0	29.8	22.35	
8.5wet 2.1dry	1.2 PD	—	—	—		
	Selegiline free base	30	30	6.0	4.5	
	Ethyl Acetate	30	30	6.0	4.5	
SEL-77C						
				(Y/E)		
	Celva 1753 (32%)	70.0	219	43.8	32.85	
14wet 2.1dry	1.2 PD	—	—	—		
	Selegiline free base	30	30	6.0	4.5	
	Ethyl Acetate	30	30	6.0	4.5	

To Page No.

Witnessed & Understood by me,	Date	Invented by	Date
		Recorded by	

TLE Formulation of patches

From Page No. with Selegiline free base

with and without 1.2 Propanediol

(#1) 1430/~~35~~ 26 1.2PD/ 15 Sel — without 1.2 PD

	~~Solids~~	liq	1/5 liq
GMS 1430 (41% sol)	85.0	207.3	69.1
1.2 PD	~~26.0~~ 0.0	0.0	0.0
Sel free base	~~13~~ 15.0	15.0	5.0
EtOH	20.0 ~~g~~	20.0 ~~g~~	10.0 ~~g~~

(#2) 1430/35 1.2PD/ 15 Sel — with 1.2 PD

	Solids	liq	1/3 liq
GMS 1430 (41%)	50.0	121.95	40.7
1.2 PD	35.0	35.0	11.7
Sel (free base)	15.0	15.0	5.0
EtOH	20.0	20.0	7.0

To Page No.

Witnessed & Understood by me, A. Hamm — Date

Invented by — Date

Recorded by Melanie

Project No.
Book No. 24 TITLE Formulation (cont)

From Page No.

(#3) 1753 / 0 1.2 PD / 15 Sel — without 1.2 PD

	solids	liqu.	1/3 liqu
Gelva 1753 (28.3%)	85.0	303.6	101.2
1.2 PD	0.0	0.0	0.0
Sel (freebase)	15.0	15.0	5.0
EtOH	30.0 liv	30.0 liv	10.0 liv

Sel was mixed with EtOH and added to 1753 while mixing.

(#4) 1753 / 35 1.2 PD / 15 Sel

~~Gelva 1753 / 35 1.2 PD / 15 Sel~~ — 1/3 liq.

	solids			
Gelva 1753	50.0	~~117.5~~ 176.7	~~75.7~~ g ~~58.9~~ 58.9	
1.2 PD	35.0	35.0	17.5	11.7
Sel (free base)	15.0	15.0	7.5	5.0
EtOH	20.0	20.0	10.0	7.0

EtOH was added to 1753
Sel was mixed with 1.2 PD and added to 1753 while mixing

To Page No.

Witnessed & Understood by me, A. Klonn | Date | Invented by | Date | Recorded by

TITLE Pec

From Page No.

Patch

#2 143

#3 195

#4 14

#5 17

Placeb

* affe

Neutral

Sel wit

Witnessed & U

Liz Cox

52

Project No.
Book No. 24 TITLE Sheer Test & peel Test

From Page No.

Sample	Adhesive weight mg/10cm²	Sheer (min)	90° peel from s/s g/in	Peel from skin (after 10 min dwell)
#1 pg 143	~~109.0~~ ~~114~~	105.2	1100	clean peel
#2 pg 143	~~125.2~~ ~~133~~	8.8	Cohesive failure	transfer to skin
#3 pg 144	~~125.0~~ ~~130~~	1362.4	650	clean peel
#4 pg 144	~~125.6~~ ~~126~~	11.4	cohesive failure	clean peel
#5 pg 147	~~122.2~~ ~~119~~	5.2	600g	transfer to skin
#6 pg 147	~~128.6~~ ~~119~~ dw dw	104.1	600g	clean peel.

Legend:

#1 1430/0 PD/15 Sel

#2 1430/35 PD/15 Sel

#3 1753/0 PD/15 Sel

#4 1753/35 PD/15 Sel

#5 1430/26 PD/11.3 Sel

#6 1753/26 PD/11.3 Sel

To Page No.

Witnessed & Understood by me, | Date | Invented by | Date | Recorded by Robert Campbell

TITLE CoA Fr

From Page No.

#		
PM3	1	1
	1	
	1	
	2	
PM3	2	
	2	
	3	
PM4	3	
	3	
	4	
PM4	4	
	4	
	5	
PM47	5	
	5	
	6	17
PM47	6	
	6	

* 1.0 m

Witnessed &

TITLE COAT WEIGHT OF FORMULATIONS #1-6 FROM PP 143-147 Book No. 24

From Page No.

	#	Formulation	Coat weight plus 1 mil PET	* 0.0315g P69 — 1 mil PET	COAT WEIGHT / 10 CM²
P143	1	1430 / 1,2 PD / 15 Sel FB	0.1392 g	0.1077	$\bar{X}$ = 113.6 MG ± 6.27 (5.5%)
	1	" " "	0.1517	0.1202	
	1	" " "	0.1445	0.1130	
P143	2	1430 / 1,2 PD / 15 Sel FB	0.1647	0.1332	$\bar{X}$ = 133.17 MG ± 0.75 (0.56%)
	2	" " "	0.1639	0.1324	
	2	" " "	0.1654	0.1339	
P144	3	1753 / 15 Sel FB	0.1612	0.1297	$\bar{X}$ = 129.97 MG ± 0.38 (0.29%)
	3	" "	0.1613	0.1298	
	3	" "	0.1619	0.1304	
P144	4	1753 / 1,2 PD / 15 Sel FB	0.1863	0.1548	$\bar{X}$ = 156.13 MG ± 1.89 (1.2%)
	4		0.1898	0.1583	
	4		0.1868	0.1553	
P147	5	1430 / 1,2 PD / 11.3 Sel FB	0.1833	0.1518	$\bar{X}$ = 148.97 MG ± 4.23 (2.8%)
	5		0.1825	0.1510	
	5		0.1756	0.1441	
P147	6	1753 / 1,2 PD / 11.3 Sel FB	0.1458	0.1143	$\bar{X}$ = 114.4 MG ± 0.36 (0.32%)
	6		0.1456	0.1141	
	6		0.1463	0.1148	

* 1.0 mil PET 0.0315g on P.69 this notebook

To Page No.

Witnessed & Understood by me, | Date | Invented by | Date

Recorded by